CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

TUBERCULOSIS INFORMATION

- Treatment of Latent Tuberculosis Infection (Preventive Therapy)

Treatment of latent TB infection (LTBI) is essential to controlling and eliminating TB in the United States. Treatment of LTBI substantially reduces the risk that TB infection will progress to disease. Certain groups are at very high risk of developing TB disease once infected, and every effort should be made to begin appropriate treatment and to ensure those persons complete the entire course of treatment for latent infection.

Who should receive treatment for latent TB infection?
Persons in the following high-risk groups should be given treatment for LTBI if their reaction to the Mantoux tuberculin skin test is ≥5mm:

- HIV-positive persons
- Recent contacts of a TB case
- Persons with fibrotic changes on chest radiograph consistent with old TB
- Patients with organ transplants, and other immunosuppressed patients (receiving the equivalent of ≥15 mg/day of prednisone for ≥1 month)

In addition, persons in the following high-risk groups should be considered for treatment of LTBI if their reaction to the Mantoux tuberculin skin test is ≥10 mm:

- Recent arrivals (< 5 years) from high-prevalence countries
- Injection drug users
- Residents and employees of high-risk congregate settings (e.g., correctional facilities, nursing homes, homeless shelters, hospitals, and other health care facilities)
- Mycobacteriology laboratory personnel
- Persons with clinical conditions that make them high-risk*
- Children < 4 years of age, or children and adolescents exposed to adults in high-risk categories

Persons with no known risk factors for TB may be considered for treatment of LTBI if their reaction to the tuberculin test is ≥15 mm. This group should be given a lower priority for prevention efforts than the groups listed above.

*HIV infection, substance abuse (especially drug injection), recent infection with *M. tuberculosis* (within the past 2 years), previous TB (in a person who received inadequate or no treatment), diabetes mellitus, silicosis, prolonged corticosteroid therapy, other immunosuppressive therapy, cancer of the head and neck, hematologic and reticuloendothelial diseases (e.g., leukemia and Hodgkin's disease), end-stage renal disease, intestinal bypass or gastrectomy, chronic malabsorption syndromes, low body weight (10% or more below the ideal)

Regimen options for treatment for latent TB infection

Isoniazid

When isoniazid is used alone to treat persons with active TB disease, resistance to isoniazid is likely to develop. For this reason, persons suspected of having TB disease should receive the recommended multidrug regimen for treatment of disease until the diagnosis is confirmed or ruled out.

Isoniazid is normally used alone for treatment of LTBI in a single daily dose of 300 mg in adults and 10-15 mg/kg body weight in children, not to exceed 300 mg per dose. Isoniazid can be given two times a week at a dosage of 15 mg/kg as directly observed therapy (DOT) of LTBI.

A 9-month regimen (minimum of 270 doses administered within 12 months) is considered optimal treatment for both HIV-positive and HIV-negative adults. A 6-month regimen (minimum of 180 doses administered within 9 months) may also provide sufficient protection. HIV-positive and HIV-negative children should receive 9 months of isoniazid treatment for infection. Twice-weekly regimens should consist of at least 76 doses administered within 12 months for the 9-month regimen and 52 doses within 9 months for the 6-month regimen. Treatment for LTBI for 6 months rather than 9 months may be more cost-effective and result in greater adherence by patients, therefore, local programs may prefer to implement the 6-month regimen rather then the 9-month regimen. Every effort should be made to ensure that patients adhere to treatment for infection for at least 6 months.

Rifampin/Pyrazinamide

Clinical trials evaluating treatment-for-latent-infection regimens shorter than 6 months and including rifampin in combination with isoniazid or pyrazinamide have been conducted among HIV-infected populations. Two- and three-month regimens with daily rifampin in combination with pyrazinamide and/or isoniazid have recently been evaluated in HIV-infected adult patients and appear to be as effective as longer courses of isoniazid. Clinical trials of this regimen in HIV-negative persons have not been conducted. Additional data are needed on acceptability and toxicity to determine if this regimen is a cost-effective alternative to longer courses of isoniazid. Regimens consisting of 2 months of rifampin and pyrazinamide are not recommended for pregnant women, because pyrazinamide's effect on the fetus is unknown.

Non–HIV-Infected Persons

The recommended 2-month treatment-of-latent-infection regimen (60 doses to be administered within 3 months) includes daily rifampin and pyrazinamide. Rifampin is given in a daily dose of 10 mg/kg (maximum dose 600 mg) and pyrazinamide is given in a daily dose of 15-20 mg/kg (maximum dose 2 g). Rifampin and pyrazinamide may also be given two times a week (16 doses to be administered for 2 months or 24 doses to be administered for 3 months). However, this regimen has not been studied in this population and should be used only when other effective regimens cannot be given. Like all intermittent regimens, this regimen must always be administered under DOT.

HIV-Infected Persons

Two-month regimens for treatment of LTBI that include rifampin or rifabutin are appropriate for HIV-positive adults who are likely to be infected with TB organisms susceptible to rifamycins.

The administration of rifampin is contraindicated with some protease inhibitors (PIs) and nonnucleoside reverse transcriptase inhibitors (NNRTIs) used for HIV therapy. For these patients, a substitution of rifabutin for rifampin is generally recommended. Clinicians are advised to consider potential drug interactions when prescribing rifamycins to patients receiving HIV therapy with PIs and NNRTIs. Daily regimens of a rifamycin (rifampin or rifabutin) and pyrazinamide should consist of at least 60 doses to be administered for 2 months or up to 3 months. This regimen may also be given two times a week (16 doses to be administered for 2 months or 24 doses to be administered for 3 months).

For HIV-positive patients receiving PIs or NNRTIs, an alternative 2-month regimen includes **rifabutin** and

pyrazinamide administered daily. However, the concurrent administration of **rifabutin** is contraindicated with hard-gel saquinavir and delavirdine. An alternative is the use of **rifabutin** with indinavir, nelfinavir, amprenavir, ritonavir, efavirenz, and possibly soft-gel saquinavir and nevirapine. Caution is advised when using rifabutin with soft-gel saquinavir and nevirapine, because data regarding the use of rifabutin with soft-gel saquinavir and nevirapine are limited. **Rifabutin** is given in a daily dose of 5 mg/kg (maximum dose 300 mg) and pyrazinamide is given in a daily dose of 15-20 mg/kg (maximum dose 2 g). The dosage of **rifabutin** may need to be adjusted when given with certain PIs and NNRTIs.

For HIV-positive patients **not** receiving PIs or NNRTIs, the recommended 2-month treatment-of-latent-infection regimen includes daily **rifampin** and pyrazinamide. **Rifampin** is given in a daily dose of 10-20 mg/kg (maximum dose 600 mg) and pyrazinamide is given in a daily dose of 15-20 mg/kg (maximum dose 2 g).

Monitoring

Baseline laboratory testing is not routinely indicated for all patients at the start of treatment for LTBI. Baseline hepatic measurements of serum AST (SGOT) or ALT (SGPT) and bilirubin are indicated for patients whose initial evaluation suggests a liver disorder. Baseline testing is also indicated for patients with HIV infection, women who are pregnant or in the immediate postpartum period (within 3 months of delivery), and persons with a history of chronic liver disease (e.g., hepatitis B or C, alcoholic hepatitis or cirrhosis, persons who use alcohol regularly, and others who are at risk of chronic liver disease). Baseline laboratory testing is not routinely indicated in older persons. However, testing may be considered on an individual basis, particularly for patients who are taking other medications for chronic medical conditions. Active hepatitis and end-stage liver disease are relative contraindications to the use of isoniazid or pyrazinamide for treatment of LTBI. Use of these drugs in such patients must be undertaken with caution.

For More Information

For more information about implementing CDC guidelines, call your state health department.

To order the following publications, call the CDC's Voice and Fax Information System (recording) toll free at (888) 232-3228, then press options 2, 5, 1, 2, 2 (Note: You may select these options at any time without listening to the complete message). Request the publication number of the document you would like to order. You may also visit the Division of TB Elimination's Web site at www.cdc.gov/nchstp/tb.

Publication # 99-6422. ATS/CDC. Targeted tuberculin testing and treatment of latent TB infection. *MMWR* 2000;49(No. RR- 6).

Publication # 99-5879. CDC. Prevention and treatment of tuberculosis among patients infected with human immunodeficiency virus: principles of therapy and revised recommendations. *MMWR* 1998;47(No. RR- 20).